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Characterization of equipment for shaping and imaging hadron minibeams

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ABSTRACT

For the feasibility studies of spatially fractionated hadron therapy prototypes of the equipment for hadron minibeams shaping and monitoring have been designed, built and tested. The collimators design was based on Monte Carlo simulations (Gate v.6.2). Slit and matrix collimators were used for minibeams shaping. Gafchromic films, micropixel detectors Timepix in a hybrid as well as metal mode were tested for measuring hadrons intensity distribution in minibeams. An overall beam profile was measured by the metal microstrip detector. The performance of a mini-beams shaping and monitoring equipment was characterized exploring low energy protons at the KINR Tandem generator as well as high energy carbon and oxygen ion beams at HIT (Heidelberg). The results demonstrate reliable performance of the tested equipment for shaping and imaging hadron mini-beam structures.

1. Introduction

Hadron therapy is preferred to conventional radiotherapy as it has a lower impact on healthy tissues in the neighborhood of the tumor being treated, see [1] and references there in.

It is expected that spatial fractionation of such beams will bring further benefits similar to those observed in biological studies with synchrotron radiation where tissue-sparing effect of arrays of parallel, narrow beams, has been established [2]. In the studies with synchrotron radiation two types of spatially fractionated beams were considered: microbeams – beam size of few tens micrometers and minibeams – few hundred micrometers (FWHM). The conceptual advantages of the spatially fractionated Hadron Mini Beam Therapy (HMBRT) exploring submillimeter wide hadron minibeams are discussed in details in Refs. [3,4]. HMBRT is expected to improve therapeutic effect for two reasons: (a) due to small beam fractions higher protection of healthy tissue is provided on the way to a tumor; (b) the dose is delivered mainly to a tumor location (Bragg peak), where beams are scattered nearly uniformly over its area/volume and are terminated there. The first positive results of the feasibility studies of HMBRT at the clinical center HIT (Heidelberg) have been reported recently in Ref. [5]. Carbon and oxygen minibeams were generated through a tungsten multislit collimator with line apertures of 700 μm separated by 3500 μm over the dose field of 1×1 cm^2. The lateral dose profiles consisted of a pattern of peaks and valleys, with Peak-to-Valley-Dose-Ratio (PVDR) comparable to ones obtained in X-rays minibeam radiation therapy. The measured PVDR values were progressively decreasing from 10–20 in the first centimeter of the phantom up to 5 at 8 cm-depth. Precise monitoring of the hadron fluence distribution over the minibeam structure is of a paramount importance for determination of the dose distribution delivered to tissue. Gafchromic films, which are normally used in conventional radiotherapy are also used for hadron beams [6]. Their off-line analysis provides excellent position accuracy (few micrometers) of the dose distribution. Yet, it is a time-consuming procedure and it does not provide on-line dose monitoring.

Previous work includes studies related to the application of position sensitive detectors for dose distribution assessment [7–9]. In particular, metal micro-pixel detectors have demonstrated reliable operation in real time even at high radiation loads [9]. In the case of high energy hadron therapy beams neither type of above-mentioned detectors (hybrid silicon pixel detectors nor metal micro-pixel detectors) provides directly

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the measurement of the dose delivered to tissue. One needs to take into account the biological effectiveness of the primary hadrons as well as the impact of secondary particles on the dose deposition. Preliminary results of previous studies [10–13] indicate that the absorbed dose is delivered mainly by the particles of the primary beam.

In this paper, we present results of tests designed to study the feasibility of spatially fractionated hadron therapy. The sizes of hadron minibeam patterns (in the range of 1 mm) as well as dose fields (1×1 cm^2) were close to ones studied in Ref. [5]. Hadron minibeam structures shaped by slit and matrix collimators optimized in Monte Carlo simulations were manufactured and characterized by micro-pixel detectors Timepix [14] using low energy protons at the KINR Tandem generator (Kyiv) as well as high energy carbon and oxygen ion beams at HIT (Heidelberg). In this way we mimicked approximately an ideal fine pencil beam.

We would like to underline, however, that spatial fractionation of the dose in clinical applications has to be provided by a scanning pencil beam to avoid additional radiation dose to the patient related to neutron and gamma generation in non-transparent parts of the beam shaping collimator. The impact of the products of nuclear reactions in the tissue to the overall dose formation is under study [15].

2. Design of the prototype equipment for feasibility studies of the spatially fractionated hadron therapy

In this work, we concentrate on two aspects related to feasibility studies of the hadron fractionated radiation therapy: shaping hadron minibeams and measuring their spatial intensity distribution. Homogeneous distribution of the dose delivered by every minibeam as well as the highest possible PVDR in healthy tissue for all beams in a multibeam structure are required to reach the expected improvement of therapeutic result. The best result would be an initially well fractionated hadron beam that is smeared on its way from the body surface to a tumor to the extent of homogeneous distribution at the tumor location.

As already mentioned, spatially fractionated hadron minibeams for clinical applications should be produced exploring technology of scanning pencil beam [4]. This is due to the fact that passive collimators, such as those applied in the case of synchrotron radiation [16] will inevitably lead to the generation of nuclear reactions products in the non-transparent parts of a collimator, in particular, neutrons and gamma-rays. Besides that, induced radioactivity in collimator material will develop with irradiation time and add additional dose on the whole patient's body.

Nonetheless, some aspects of the HMBRT development could be studied using collimators for shaping minibeam structures by slit or matrix collimators [3–5]. One of them aims at the verification of the Monte Carlo simulations of the lateral hadron intensity distribution over the depth in a phantom. The optimization of the minibeams size and pitch, collimator material and thickness and its distance to phantom is required for finding the highest value of the Peak-to-Valley-Hadron-Intensity-Ratio (PVHIR). The minimal thickness of a collimator was determined by the range of hadrons in a collimator material. We kept it at this level to reduce the contribution of ions scattering by the collimators walls into valleys range. Preliminary evaluations show that PVHIR are correlated with the PVDR defined as the ratio between the central dose of one minibeam (peak dose) and the dose in the middle of two consecutive beams (valley dose). The uncertainty of PVDR is determined by statistical fluctuation of the beam intensity which in this study was in the range of 10%. Another factor of uncertainty in the delivered dose arises from the impact of nuclear reaction products generated by hadron interactions with the phantom's (human body's) nuclei. For instance, fragmentation of nuclei produces neutrons, gamma-rays, alpha-particles etc. with energies which are high enough to proliferate through the whole body. This has to be thoroughly studied, both theoretically and experimentally. Studies with gafchromic films [5] show that smearing of the spatial fractionation of the hadron minibeams increases significantly with depth in the phantom. The relative contribution to this phenomenon of hadrons elastically scattered at the collimator edges and nuclear reactions products could be studied by exploring the sensitivity of the Timepix detector to different charged particles [13].

Table 1
PVDR calculated for different depth in a water phantom for slit collimators made out of brass, lead and aluminum. Proton energy 105 MeV. Distance between phantom and collimator—20 cm.

Depth in phantom (cm)	Brass, PVDR	Lead, PVDR	Aluminum, PVDR
1	40.0 ± 3.0	38.0 ± 2.0	47.0 ± 3.0
2	32.0 ± 2.0	34.0 ± 2.0	36.0 ± 2.0
3	21.0 ± 1.0	20.0 ± 1.5	24.0 ± 1.5
4	15.0 ± 1.0	10.0 ± 1.0	10.0 ± 1.0
5	11.0 ± 1.0	4.0 ± 0.4	6.0 ± 0.5
6	4.0 ± 0.5	2.0 ± 0.2	3.0 ± 0.3
7	2.0 ± 0.2	2.0 ± 0.2	2.0 ± 0.2

A simplified approach to shaping the spatially fractionated dose field is described in this paper. Minibeams are assumed to be shaped by slit and matrix collimators made out of different metals. Design of collimators and their efficacy were evaluated by Monte Carlo simulations in the framework of a software package for medical physics "Gate v.6.2" [17]. Some preliminary results were published earlier [18,19]. The PVDR value and its evolution over the phantom thickness was an important criteria used to determine the efficacy of the dose deposition. The PVDR depends on the material, width/pitch ratio and distance between collimator and phantom. The scattering of hadrons by the slit edges makes fractionation less pronounced for large distances. Evaluations were made for water phantom with field sizes (2×2) cm^2 and collimators manufactured out of aluminum, brass and lead. The width of the slits was assumed to be 0.7 mm, while the center-to-center (c-t-c) distance was varied from 1.4 mm to 2.8 mm in steps of 0.7 mm. Calculations were made for hydrogen, carbon and oxygen ion beams with energies region of 80–250 MeV/nucleon, relevant for medical applications.

As an example, Fig. 1 shows the results of the simulations of the lateral dose distribution delivered at different depths in a water phantom by hydrogen ions minibeams with energy of 105 MeV passing through the slits in a brass collimator (thickness: 20 mm, five slits with a width of 0.7 mm, c-t-c distance: 2.8 mm).

Calculations were performed assuming a primary proton beam with rectangular shape of 20×20 mm^2, Gaussian energy distribution (FWHM = 0.5 MeV), beam divergence of 1 mrad in horizontal and vertical direction, both. Calculations show that PVDR drops down from 40 to 2 at phantom depths of 1 cm and 5 cm, respectively. For the fixed distance between the phantom and collimator PVDR goes down with a thickness of a collimator due to the scattering of the beam at the collimator holes surface.

Similar calculations were made for the aluminum and lead collimators with thickness of 40 and 13.9 mm, correspondingly. Results are summarized in Table 1. Analyzing these results as well as calculations made for carbon and oxygen ions (including results for matrix collimators), we conclude that PVDR drops down significantly as a function of the depth in the phantom, approaching to homogeneous dose distribution at the targeted depth of assumed tumor location. For instance, calculations show that with the layout of 1 mm wide slits and c-t-c distance between them of 2 mm the brass collimator provides spatially homogeneous distribution of the delivered dose at the depth in phantom of 5 cm. Thus, optimal shaping of minibeams with slit or matrix collimators is possible to fulfill also the goal of de-fractionation of the dose at the tumor location.

3. Test of the equipment for shaping and monitoring of hadron minibeams

Based on the Monte Carlo simulations, different collimators were manufactured out of metal plates of aluminum, brass and tungsten. Slit